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EXAMINER

ZITOMER, STEPHANIE W

ART UNIT PAPER NUMBER

1655

DATE MAILED: 01/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/752,293

Applicant(s)
CHENCHIK et al.

Examiner
S. Zitomer

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1655



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jan 29, 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3 20) ☐ Other: _____

DETAILED ACTION

Rejections under 35 U.S.C. 112, second paragraph: Indefiniteness

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) In claims 1-18 and 22-25 the term "representative number" in claims 1, 6, 13 and 22 is a relative term which renders the claims indefinite. The term "representative number" is not defined by the claim and the specification does not provide a standard for ascertaining the requisite "representative" number. Therefore, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(b) Claims 1-18 and 22-25 are indefinite because the term "representative" is *non sequitur* to the method and method embodiments of the claims and is not defined in the claims or in the specification as to what is "represented".

(c) Claims 6-12 are confusing in missing the word "acid" after "nucleic" in line 2.

(d) Claims 6-12 are confusing in that claim 6 does not appear to be further limiting of claim 1. Claim 1 recites that the tagged target nucleic acids are generated with tagged primers, i.e., by enzymatic primer extension which appends the tag to the nucleic acid copy. If applicant is aware of nonenzymatic means of generating nucleic acids with primers such information should be provided as it may raise a written description issue. If not, claim 6 should be canceled or combined with claim 1.

(e) Claims 13-18 lack antecedent basis in (a) for (b) because the latter recites means involving **both** the array and the set of tagged gene specific primers whereas (a) recites only one of them. It is suggested to recite that both (i) and (ii) are present in (a) by combining claims 13 and 14.

(f) Claim 20 is confusing in that it does not appear to be further limiting of claim 19. Claim 19 recites that the tag and tag complement **hybridize** and therefore are taken to be nucleic acids. See above at (d).

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Rejections under 35 U.S.C. 102(e): Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

2. Claims 1, 2, 5, 6 and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by the patent to Brenner (5,863,722). Regarding claims 1 and 2, Brenner discloses the claimed invention hybridization assay comprising the steps of (a) generating a population of tagged target nucleic acids from an initial sample with a collection of tagged gene specific primers wherein the tagged target nucleic acids are labeled; (b) contacting the population of tagged target nucleic acids with an array of tag complements immobilized on a solid support; (c) detecting any resultant hybridization complexes on the array wherein the initial sample comprises RNA (columns 36-37, claim 1; column 14, lines 37-41). Regarding claim 5, Brenner discloses that the tagged target nucleic acids are labeled (column 19, lines 38-46; column 17, lines 1-13). Regarding claim 6 wherein the generating in claim 1 comprises an enzymatic non-amplification primer extension, the patent discloses this embodiment (column 14, lines 37-41). Regarding claim 11 wherein the initial nucleic acid is RNA, the patent discloses this embodiment (column 14, lines 37-41).

3. Claims 1, 2, 5, 6, 11 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by the patent to Kamb et al. (6,060,240). Regarding claims 1, 2, 5, 11 and 12, Kamb et al. disclose the claimed invention hybridization assay comprising the steps of (a) generating a population of tagged target nucleic acids from an initial sample with a collection of tagged gene specific primers wherein the tagged target nucleic acids are labeled; (b) contacting the population of tagged target nucleic acids with an array of tag complements immobilized on a solid support; (c) detecting any resultant hybridization complexes on the array wherein the initial sample comprises RNA (claim 1; column 7, lines 53-55; column 15, lines 41-50). Regarding claim 6 wherein the generating in claim 1

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comprises an enzymatic non-amplification primer extension step, the patent discloses this embodiment (column 9, lines 49-52).

Rejections under 35 U.S.C. 103(a): Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 3, 4 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner as applied to claims 1, 2, 5, 6 and 11 above (paragraph 3), and further in view of Shannon et al. (6251,588) and Lockhart et al. (6,333,155). The claim 1 method embodiments of claims 3, 4 and 7-10 differ from that of Brenner wherein any difference in hybridization efficiency between any two tag/tag complements does not exceed about 10 fold (claim 3), about 5 fold (claim 7) or about 3 fold (claim 8) and wherein the level of cross-hybridization of any tag employed in the method does not exceed about 10% (claim 4), about 2% (claim 9) or about 1% (claim 10). However, Brenner teaches selecting the tag oligonucleotides from a minimally cross-hybridizing set (column 2, lines 47-54; column 6, line 16-column 7, line 44). Furthermore, the practice of minimizing cross-hybridization thereby optimizing hybridization efficiency in the use of nucleic acid arrays was routine in the art at the time the claimed invention was made. For example, Shannon et al. provide a description of the prior art on the topic as well the rationale for optimizing hybridization efficiency of oligonucleotides in arrays (column 2, line 52-column 6, line 19). Lockhart et al. address the need for optimizing the hybridization efficiency of oligonucleotides in an array as well as the problem of cross-hybridization: "it is recognized that hybridization efficiency

varies with base composition and probe length" (column 14, lines 63-64) and "oligonucleotide probes in the high density array are selected to bind specifically to the nucleic acid target to which they are directed with minimal non-specific binding or cross-hybridization" (column 15, lines 64-67). Therefore, it would have been obvious and the skilled practitioner in the art at the time the claimed invention was made would have been motivated to select tag/tag complements having hybridization efficiencies with minimal differences and minimal cross-hybridization for the known benefit of maximizing hybridization results. In *In re Aller*, 105 USPQ 233, the court found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results.

5. Claims 3, 4 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamb et al. as applied to claims 1, 2, 5, 6, 11 and 12 above (paragraph 4), and further in view of Shannon et al. (6,251,588) and Lockhart et al. (6,333,155). The claim 1 method embodiments of claims 3, 4 and 7-10 differ from that of Kamb et al. wherein any difference in hybridization efficiency between any two tag/tag complements does not exceed about 10 fold (claim 3), about 5 fold (claim 7) or about 3 fold (claim 8) and wherein the level of cross-hybridization of any tag employed in the method does not exceed about 10% (claim 4), about 2% (claim 9) or about 1% (claim 10). However, Kamb et al. teach minimizing cross-hybridization among the tags to promote hybridization efficiency (column 15, lines 51-53; column 16, lines 10-15). Furthermore, the practice of minimizing cross-hybridization and optimizing hybridization efficiency in the use of nucleic acid arrays was routine in the art at the time the claimed invention was made. For example, Shannon et al. provide a description of the prior art on the topic as well the rationale for optimizing hybridization efficiency of oligonucleotides in arrays (column 2, line 52-column 6, line 19). Lockhart et al. address the need for optimizing the hybridization efficiency of oligonucleotides in an array as well as the problem of cross-hybridization: "it is recognized that hybridization efficiency varies with base composition and probe length" (column 14, lines 63-64) and "oligonucleotide probes in the high density array are selected to bind specifically to the nucleic acid target to which they are directed with minimal non-specific binding or cross-hybridization" (column 15, lines 64-67). Therefore, it would have been obvious and the skilled practitioner in the art at the

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time the claimed invention was made would have been motivated to select tag/tag complements having hybridization efficiencies with minimal differences and minimal cross-hybridization for the known benefit of maximizing hybridization results. In *In re Aller*, 105 USPQ 233, the court found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results.

6. Claims 13-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner in view of Burmer (6,087,103), Shannon et al. (6,251,588) and Lockhart et al. (6,333,155) as applied to claims 1-12 above (paragraphs 3 and 4) and further in view of Brown et al. (Nat. Gen. Suppl. 21:33-37, Jan. 1999). Regarding claims 13-18, the claimed invention differs from the disclosure of Brenner wherein are provided in kit form (claims 13-18) and separately a tag complement array (claims 19-21) and a set of tagged gene specific primers (claims 22-25) wherein the kit further comprises means for identifying the array location to which each tag hybridizes. Brenner discloses an array of distinct tag complements immobilized on the surface of a solid support (column 35, claim 1) having means for identifying the physical location on the array where the tagged primer hybridizes (column 9, lines 20-34) and sets of DNA identifier tags attached to gene specific primers (column 14, lines 37-41). The claimed arrays and sets of claims 13-18 differ from those of Brenner in being in a kit. However, in an assay in which tagged nucleic acids are immobilized on a solid support via hybridization of the tags with tag complements in an array on the solid support, Burmer teaches kits comprising at least one of an array of distinct tag complements immobilized on the surface of a support and a set of distinct tagged nucleic acids (tag library and target library) (column 15, lines 8-15; column 7, lines 35-36) plus a means for identifying the physical location on the array to which each distinct tagged affinity ligand hybridizes, i.e., spacial positioning (column 15, lines 8-15; column 11, lines 15-23). It would have been obvious and the skilled practitioner in the art would have been motivated at the time claimed inventions were made to provide the array of tag complements and the set of tagged primers disclosed by Brenner in a kit for the known benefit of commercial applications and ease of performance of claimed invention method. The claimed invention arrays and sets further differ from those of Brenner in the embodiments of claims 15, 16, 19 and 22-25 wherein the magnitude of difference in

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hybridization efficiency between any two tag/tag complement pairs does not exceed about 10 fold and any tag in the set of tagged affinity ligands has a level of cross-hybridization with respect to the array that does not exceed 10%. However, Brenner teaches selecting the tag oligonucleotides from a minimally cross-hybridizing set (column 2, lines 47-54; column 6, line 16-column 7, line 44). Furthermore, the practice of minimizing cross-hybridization and thereby optimizing hybridization efficiency in the use of nucleic acid arrays was routine in the art at the time the claimed invention was made. For example, Shannon et al. provide a description of the prior art on the topic as well the rationale for optimizing hybridization efficiency of oligonucleotides in arrays (column 2, line 52-column 6, line 19). Lockhart et al. address the need for optimizing the hybridization efficiency of oligonucleotides in an array as well as the problem of cross-hybridization: "it is recognized that hybridization efficiency varies with base composition and probe length" (column 14, lines 63-64) and "oligonucleotide probes in the high density array are selected to bind specifically to the nucleic acid target to which they are directed with minimal non-specific binding or cross-hybridization" (column 15, lines 64-67). Therefore, it would have been obvious and the skilled practitioner in the art at the time the claimed invention was made would have been motivated to select tag/tag complements having hybridization efficiencies with minimal differences and minimal cross-hybridization for the known benefit of maximizing hybridization results. In *In re Aller*, 105 USPQ 233, the court found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results. Regarding claims 17 and 18, the claimed invention kit differs from that of Brenner in view of Burmer wherein the means for identifying the physical location on the array comprises a medium that includes identifying information or a means for remotely assessing the information is provided in the kit wherein the latter is a website address. However, it would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to include printed information such as a website address in the kit in view of routine practice in the art of accessing public nucleotide sequence databases for sequence searching for the obvious benefit of obtaining a large amount of sequence information in a readily available format. For example, Brown et al. teach that the use of molecular arrays

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generates a large amount of information which may be managed and published via websites. Regarding claim 21, the claimed invention array differs from that of Brenner wherein the array has a density that does not exceed about 400 spots/square cm. However, oligonucleotide arrays routinely used in the prior art were known to have densities ranging from less than 100 to more than 1000 spots per square cm. Therefore, one of ordinary skill in the art at the time the claimed invention was made would have been motivated according to personal preference to select an array density appropriate to particular experimental parameters for the obvious benefit of optimizing results. Regarding claim 25, the claimed invention set of tagged affinity ligands comprises at least 20 distinct tagged ligands. However, the skilled practitioner in art would have selected the number of tagged primers based on personal preference and experimental considerations. For example, Burmer teaches this embodiment in Figure 1.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 8:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.


Stephanie Zitomer, Ph.D.

January 28, 2002

STEPHANIE ZITOMER
PATENT EXAMINER